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Complete resolution of right atrial free-floating thrombus after warfarin therapy in chemotherapy-induced cardiomyopathy: a case report

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Case Report

ABSTRACT

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Free-floating right heart thrombus is a rare phenomenon and has dismal prognosis. The optimal management of free-floating right thrombus remains controversial with no clear consensus. We present a case of right atrial free-floating thrombus in 56-year-old woman in chemotherapy induced-cardiomyopathy. Three weeks of warfarin treatment showed complete thrombus resolution. To the best of our knowledge, no such case has previously been reported in Indonesia.

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Trombus yang bergerak bebas di jantung bagian kanan jarang ditemukan dan memiliki prognosis yang buruk. Belum ada pedoman resmi mengenai tatalaksana yang optimal untuk kasus tersebut dengan pilihan terapi yang masih kontroversial. Kami melaporkan sebuah kasus dari seorang pasien perempuan, umur 56 tahun dengan kardiomiopati akibat kemoterapi dan trombus yang bergerak bebas di atrium kanan. Setelah pemberian warfarin selama tiga minggu, trombus tersebut tidak ditemukan lagi. Sejauh pengetahuan kami, belum ada kasus seperti ini yang dilaporkan di Indonesia.

INTRODUCTION

Free-floating right heart thrombus (FRHT) is a rare phenomenon and associated with potentially fatal pulmonary embolism (PE).^{1,2} Looking at the literature there is no clear consensus on therapeutic management. Some authors think that surgical embolectomy is the most efficient treatment,³ some favor thrombolysis,^{4,5,6} some treat by intuition only,⁷ and a few use heparin only when surgery or thrombolysis are contraindicated.^{3,4} We present a case of a patient with right atrial free-floating thrombus in chemotherapy induced-cardiomyopathy who was treated successfully with warfarin without embolic complication. To the best of our knowledge, this is the first report in Indonesia.

Case Presentation

A 56-year-old woman presented to our department with dyspnea. She was admitted with symptoms and signs of congestive heart failure. Her past medical history revealed that she underwent simple mastectomy for breast cancer 6 years ago. Postoperatively she treated with adjuvant chemotherapy with cyclophosphamide, doxorubicin, and 5-Fluorouracil. Laboratory data showed elevated D-dimer (1,3 µg/ml, normal value <0,5 µg/ml). ECG showed sinus tachycardia, right atrial enlargement and LVH. Transthoracic echocardiography (figure 1;A) was performed, demonstrating an ovoid-shape, mobile thrombus

(31x29 mm) in the right atrium, dilated all cardiac chambers with global hypokinesia. Thorax computed tomography with contrast showed filling defect in anterior wall of right atrium, suggesting a right atrial thrombus. No thrombosis was detected at venous doppler ultrasound. Anticoagulation therapy with

warfarin (2 mg o.d.) was initiated, dose adjusted to maintenance INR 2 – 3. Following warfarin administration, weekly echocardiography examination demonstrated gradual decreases in the thrombus size. After three weeks, no thrombus was detected (figure 1; D) and no pulmonary embolism had occurred.

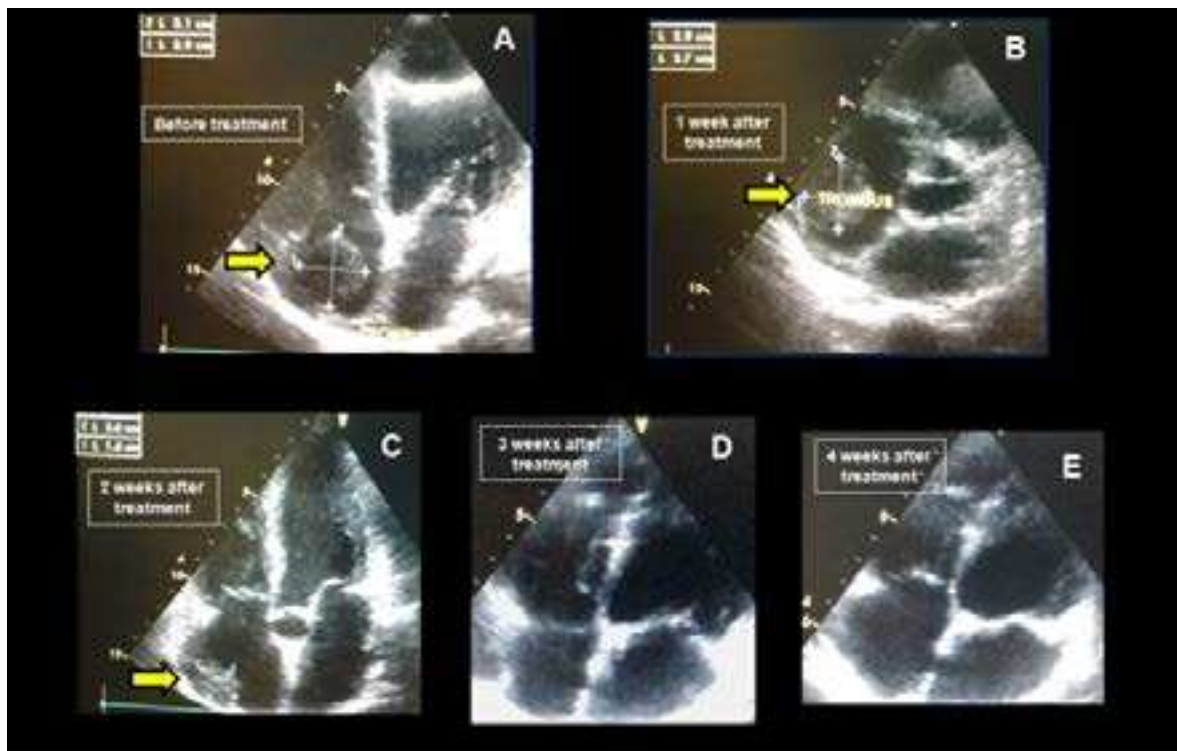


Figure 1. Thrombic progression in right atrium (thrombus indicated by arrow)

(A) Prior anticoagulation therapy, thrombus size was 21x39mm. **(B)** One week after initial warfarin administration (2mg o.d), thrombus size was 29x27mm. **(C)** Two weeks after treatment, thrombus size was 20x16mm. **(D)** Three weeks after treatment, thrombus was undetectable. **(E)** Four weeks after treatment, thrombus still undetectable

DISCUSSION

FRHT is uncommon and associated with worse outcome since it is an indication of imminent and potentially fatal PE.^{1,2} In patient with FRHT, the incidence of PE is 97% and reported mortality is over 44%.^{2,8}

The two major etiologies of right heart thrombus are embolic (due to propagation of a deep vein thrombosis, DVT) or in situ (due to stagnant blood flow, as seen in cardiomyopathy and in arrhythmia, such as in atrial fibrillation). However, there are case reports documenting right heart thrombus secondary to pacemaker wires⁹, central venous catheters¹⁰, hemodialysis catheters¹¹, and embryological remnants¹², as a

complication of ablation¹³, formed during cardiac arrest with cardiopulmonary resuscitation¹⁴, and after carbon monoxide poisoning¹⁵. With regard to our patient, it is likely that the FRHT development was multifactorial. She had history of simple mastectomy and chemotherapy for breast cancer with cyclophosphamide, doxorubicin, and 5-Fluorouracil. Malignant disease is associated with hypercoagulability with increased incidence of thromboembolism.¹⁶ Kim et al¹⁷ reported that doxorubicin significantly increased phosphatidylserine and subsequently induced platelet procoagulant activity, which could ultimately contribute to the increased thrombus formation. Dilated cardiac chambers with global hypokinesia of our patients suggested

a chemotherapy-induced cardiomyopathy that supported by echocardiography result that performed before chemotherapy. It revealed normal cardiac chambers with global normokinesia. Topoisomerase (Top)2-alpha (overexpressed in tumors) is the cellular target for the drug's anticancer effect. DNA damage via Top2-beta (expressed in adult cardiomyocytes) leading to cardiomyocyte death has recently been implicated as a major mechanism of doxorubicin-related cardiomyopathy.¹⁸ Malignant disease, use of chemotherapy agent and dilated of cardiac chambers with global hypokinesia are contributing factors for thrombus formation in our patient.

Right heart thrombus morphology has been separated into three types based on results from a multicenter questionnaire on echocardiographically detected right heart thrombus¹⁹: type A - thin, highly mobile, serpiginous (worm-like shape), and mostly represent peripheral venous clots which temporarily lodge into the right heart; type B - less mobile, ovoid shaped, attach to the right atrial or ventricular wall, have broad-based attachment indicating that these develop within the right heart; type C - had characteristics of both A and B (highly mobile but globular). Type A thrombi were mostly associated with DVTs, type B thrombi were mostly associated with low-flow states, and type C thrombi included a combination of both. By the appearance of echocardiography result and no evidence of DVT (clinically and venous doppler ultrasound as well), she most likely had a type B thrombus.

The optimal management of FRHT remains unclear despite the availability of several different modalities of treatment including anticoagulation with heparin, thrombolysis, catheter embolectomy, and surgical embolectomy.^{19,20} Surgical embolectomy has its own set of potential complications including an inherent delay of at least hours, general anesthesia, cardiopulmonary bypass, and the inability to remove coexisting pulmonary embolism beyond the central pulmonary arteries. One of the major advantages of the surgical approach is the ability to simultaneously repair a patent foramen

ovale, thus reducing the risk of a subsequent paradoxical embolism. In contrast, thrombolytic therapy can be administered quickly and results in the simultaneous thrombolysis of cardiac and pulmonary arterial thromboemboli as well as thrombus in the femoral venous circulation.²⁰ Thus, thrombolysis may be initially advocated.^{7,21} However, there have been several cases of sudden death reported with thrombolytic therapy,²² which may be due to thrombus fragmentation.²³ Moreover, fragmented thrombi could cause chronic pulmonary hypertension.^{24,25}

FRHT is an extreme therapeutic emergency and any delay to treatment could be lethal.¹⁹ Investigators reported on a series of 38 consecutive patients with FRHT that 21.1% of the patients died within the first day after admission. They have recommended either urgent surgical treatment or thrombolysis of mobile right heart thrombus, although prospective data of optimal treatment are lacking.² Our patients was denied surgical intervention and not treated with thrombolytic therapy because of the risk of embolization of large thrombus fragments. Interventional techniques using basket device to trap the thrombus into the inferior vena cava with placement of caval filter above the thrombus has been described previously² but we do not have experience with this procedure. However, our patient responded very well to oral anticoagulation with warfarin, a coumarin derivative, produces an anticoagulant effect by interfering with the cyclic interconversion of vitamin K and its 2,3 epoxide (vitamin K epoxide).²⁶ Three weeks of warfarin treatment showed complete thrombus resolution without embolic complication.

CONCLUSION

The right atrial free-floating thrombus resolved after warfarin administration. The most appropriate therapeutic approach for managing right heart thrombi remains to be determined, but our data suggest that oral anticoagulant therapy with warfarin is effective and readily available.

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